REMARKS

The Response

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 47, 49, 50, 52, 53, 59-68, and 71-101 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. In particular, the Examiner asserts that the specification does not adequately describe the nexus between the activity of c-Met activity and a useful treatment of a disease or condition. The Examiner also contends that it would not be predictable that the claimed methods would function as contemplated and that it would require undue experimentation by one of skill in the art to practice the invention. Applicants traverse.

In the Reply to Office Action filed on May 16, 2007 (hereafter, "the May Reply"), applicants presented evidence that a link between c-Met kinase activity and various cancers was established at the time of the invention. Applicants also presented evidence that a small molecule c-Met inhibitor was shown to have antitumor effects in an *in vivo* model. See the arguments presented in the May Reply relating to paragraphs [0048] to [0050] on pages 14-15 of the specification; Heideman et al., J. *Gene Medicine* 6: 317-327, 2004; Tomioka et al., *Cancer Res.* 61: 7518-7524, 2001; Saga et al., *Gene Therapy* 8: 1450-1455, 2001; Martin et al., *Carcinogenesis* 24(8): 1317-1323, 2003; Davies et al., *Int. J. Cancer* 106: 348-354, 2003 and Christensen et al., *Cancer Res.* 63: 7345-7355, 2003. The cited specification text and these references clearly show that at the time the invention was made, there was a reasonable correlation between the activation of c-Met in various cancers, the use of a c-Met inhibitor to inhibit cancer cell growth, and the use of the c-Met inhibitors of the invention to treat the cancers recited in claim 52. Applicants also argued in the May Reply that a skilled artisan would be able to discern an appropriate dosage and method of use based upon the information provided in the specification (see paragraphs [00142] to [00143] on pages 49-50) along with the general knowledge of one skilled in the art.

When analyzing the breadth of the claims in the instant Office Action, the Examiner states that the claims are drawn to the treatment of any and all disease mediated by c-Met with the compounds of formula I. This is incorrect. Claim 52, the broadest method of treatment claim, recites a method of using a composition of the invention to treat a cancer selected from gastric cancer, pancreatic cancer, ovarian cancer, breast cancer, or prostate cancer. The Examiner also does not differentiate the subject matter of claim 52 from that of claim 50, which recites an *in vitro* method of inhibiting c-Met activity in a biological sample selected from a cell culture, biopsied material obtained from a mammal, saliva, urine, feces, semen, or tears, or an extract thereof.

Further, the Examiner states that the arguments presented in the May Reply are not persuasive because the pharmaceutical arts are unpredictable, requiring each embodiment to be individually assessed for physiological activity and that this individual assessment is necessary because the therapeutically useful *in vivo* activity of any compound depends to a great extent on the pharmacokinetic/pharmacodynamic parameters, as well as the therapeutic index of that particular compound. These assertions do not meet the burden of establishing a reasonable basis to question the enablement provided for the claimed invention.

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support [emphasis added]. See *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent

with the contested statement" [emphasis added]. See the Manual of Patent Examination Procedure (MPEP) § 2164.04.

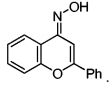
The Examiner has offered no such evidence. The Examiner has presented nothing that contradicts applicant's evidence and rationale that the *in vitro* data presented correlates to an *in vivo* use of the compositions of the invention for the treatment of the cancers recited in claim 52 or the *in vitro* use of the compositions of the invention in the inhibition of c-Met activity in various biological samples. As stated in MPEP § 2164.02: "'[c]orrelation' refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed or claimed method invention . . . .In this regard, the issue of 'correlation' is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate [emphasis added]. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications)."

Applicant's presentation of evidence in the May Reply demonstrate that the claims are enabled because there is a nexus between the *in vitro* data presented in the specification and the *in vivo* properties of similar compositions known to those skilled in the art at the time the invention was made. The Examiner has not overcome the burden of showing a lack of correlation between *in vitro* behavior of the compounds of the invention and the pharmaceutical compositions of claims 47, 49, 59-68, 71-101; the *in vitro* method of inhibiting c-Met activity in a biological sample recited in claim 50; and the methods of treating various cancers with the compositions of the invention recited by

claim 52 and 53. Accordingly, applicants respectfully request that the rejection of claims 47, 49-50, 52-53, 59-68, and 71-101 under U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. § 102(b)

The Examiner has rejected claim 47, and claims dependent thereon, under 35 U.S.C. § 102(b) for allegedly being anticipated by Gulati et al., *Current Science* 5: 75, 1936 (hereafter, "Gulati"). In particular, the Examiner asserts that Gulati teaches the following compound:



Applicants traverse. In order for a reference to anticipate a claim under U.S.C. § 102(b), it must teach each and every element as set forth in the claim. See § 2131 of the MPEP. The instant claims recite pharmaceutical compositions and methods of using the pharmaceutical compositions, wherein the compositions comprise the recited compounds of formula **I** and a pharmaceutically acceptable carrier, adjuvant, or vehicle. Gulati describes a method of preparing the compound indicated above but does not describe or suggest its use as part of a pharmaceutical composition, a method of inhibiting c-Met activity *in vitro*, or methods of treating various forms of cancer. Accordingly, applicants respectfully request that the rejection of claim 47, and claims dependent thereon, under U.S.C. § 102(b) be withdrawn.

Conclusion

Applicants request that the Examiner consider the remarks herein and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the undersigned be contacted at the Examiner's convenience.

Respectfully submitted,

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